

**REMARKS:**

**I. Status of the Claims**

Claims 57, 58, and 62-70 are pending, and claims 1-56 and 59-61 are canceled. By this amendment claim 67 is amended. The claim amendments do not add new matter and are supported by the specification.<sup>1</sup>

The Applicant acknowledges with appreciation withdrawal of claim objections and withdrawal of the §§ 102 and 103 rejections in view of CAS reg. no. 59101-30-3.

**II. Summary of the Invention**

It is well known in the art that most ionic salts are solids in which the ions that make up the salt form a crystalline lattice. Such solid salts may be soluble in aqueous solvents (e.g., water) or organic solvents. The solvent in which the solid salt is dissolved contains the solvent molecules and the ions of the salt which are solvated by the solvent. **A few ionic salts, rather than forming a solid crystalline lattice, take the form of a liquid. The ions that make up the salt are not in solution (i.e., are not solvated), but rather they are present as the ions themselves. The liquid is composed solely of the ions that make up the ionic salt. Such salts are known as ionic liquids.** Ionic liquids generally have high melting points above which they are liquid and below which they are solid. Salts that form ionic liquids and have low melting points are rare; those that are liquid at room temperature (25°C) are rarer still. The present invention provides salts that form ionic liquids at room temperature and methods of using these unique ionic liquids as solvents in various applications.

**III. 35 U.S.C. § 103 Rejections**

Reconsideration is respectfully requested of the rejections of claims 57, 58, and 62-70 under 35 U.S.C. § 103(a) in view of Rogier et al. (US 2003/0232844).

Claim 57 is directed to a method for using an ionic liquid in a variety of applications in which the cation of the ionic liquid is a tertiary ammonium ion of the formula  $N^+HRR'R''$  wherein R is an alkyl group substituted with one or more hydroxyl

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<sup>1</sup> Support for the amendments to claim 67 may be found in published paragraphs [0029], [0230], [0310], and [0311].

groups, and R' and R" are independently alkyl or substituted alkyl groups. Claim 58 is directed to a method for carrying out an enzyme-catalyzed reaction in which the liquid reaction medium in which the reaction is conducted comprises an ionic liquid as defined above. Ionic liquids are unique salts that exist as stable liquids above their melting point. An ionic liquid contains only the ions making up the salt (the liquid does not contain any solvent molecules). A typical salt dissolved in a solvent such as water **is not** an ionic liquid.

Rogier et al. disclose new compounds for use in treating COX-2 mediated disorders, wherein the new compounds have a structure of Formula I-IV as defined by Rogier et al. At paragraph [0627] Rogier et al. disclose salts of the new compounds of Formulas I-IV. The salts may be either formed from an acid or from a base depending on the nature of the new compound, i.e., whether the compound of Formula I-IV has a basic or acidic group with which to form a salt. Rogier et al. list compounds from which such salts may be formed; 2-dimethylaminoethanol is listed as a possible base and formic acid is listed as a possible acid. Thus, Rogier et al. are disclosing the 2-dimethylaminoethanol salt of their compound of Formula I-IV and the formate salt of their compound of Formula I-IV. Nowhere do Rogier et al. disclose or suggest reacting 2-dimethylaminoethanol with formic acid. Even if these ions were reacted, however, they would form dimethylaminoethanol formate. Dimethylaminoethanol formate is an amine salt. More importantly, the ammonium salt N,N-dimethylethanolammonium formate would not be formed. N,N-dimethylethanolammonium formate is an ionic liquid.

Claims 57 and 58, however, are directed to methods for using an ionic liquid in an application, such as, e.g., as a solvent or reaction medium in an enzyme-catalyzed reaction. Nowhere do Rogier et al. disclose or suggest using a salt of one of their compounds of Formulas I-IV or a salt such as dimethylaminoethanol formate as a solvent in an enzyme-catalyzed reaction. The Office states that Rogier et al. teach "application of an enzyme such as a protease on a substrate [0030]. It is well known that the protease enzyme catalyzes a reaction with protein."<sup>2</sup> The Applicant does not dispute the observation that the metallomatrix protease disclosed by Rogier et al.

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<sup>2</sup> Office action dated 2/17/2011, at page 2, last paragraph.

catalyzes a reaction with a protein, but Rogier et al. fail to disclose or suggest using a salt of one of their compounds of Formulas I-IV or a salt such as dimethylaminoethanol formate as the solvent (or reaction medium) in an enzyme-catalyzed reaction. Although not noted by the Office, Rogier et al. disclose a COX-mediated enzyme reaction in which a COX enzyme was “incubated in a potassium phosphate buffer (50 mM, pH 8.0) containing epinephrine, phenol, and heme with the addition of arachidonic acid.”<sup>3</sup> This reaction, therefore, is performed in the presence of potassium phosphate buffer and not an ionic liquid as required in claims 57 and 58.

The Office states that Rogier et al. disclose the “salts may be part of a solution [0623, 0717].”<sup>4</sup> Paragraphs [0623] and [0717] of Rogier et al. disclose that, for therapeutic purposes, the compounds of the invention may be combined with appropriate adjuvants. For example, the compounds of Formulas I-IV (or salts thereof) may be dissolved in water or other solutions for parenteral administration. Neither of the cited passages discloses or suggests using a salt of one of their compounds of Formulas I-IV or a salt such as dimethylaminoethanol formate as the solvent in an enzyme-catalyzed reaction. The ionic liquids of the present invention are unique in that they are liquids at room temperature and **DO NOT** have to be dissolved in a solution to be utilized.

The Office states “the present claims would have been obvious in view of the teaching of Rogier because it teaches both the cation and anion from a limited number of choices for use in compositions for applying an enzyme to a substrate.”<sup>5</sup> As detailed above, Rogier et al. do not disclose or suggest combining dimethylaminoethanol and formate, rather they disclose forming salts of a compound of Formula I-IV by reacting the compound of Formula I-IV with a base (e.g., dimethylaminoethanol) or an acid (e.g., formic acid). Even if a person skilled in the art were somehow motivated by the disclosure of Rogier et al. to react dimethylaminoethanol with formate, there is no suggestion in Rogier et al. or in the knowledge generally available to those skilled in that art to use the resultant salt (dimethylaminoethanol formate) as the solvent or the

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<sup>3</sup> Rogier et al., at paragraphs [0704] and [0706] (emphasis added).

<sup>4</sup> Office action at page 4, first full paragraph.

<sup>5</sup> *Id.*, at page 3, second paragraph.

reaction medium for an enzyme-catalyzed reaction. As exemplified in the Examples of Rogier et al., enzyme-catalyzed reactions typically are performed in the presence of buffers or reaction solutions that mimic the normal physiological surrounding of the enzyme of interest (e.g., a buffered potassium phosphate solution). Simply stated, neither the disclosure of Rogier et al. nor knowledge generally available to those skilled in the art provides a reason or a suggestion to modify the disclosure of Rogier et al. to arrive at the method of using an ionic liquid as a solvent in an enzyme-catalyzed reaction with a reasonable expectation of success.

As detailed above in section II, ionic liquids are salts that exist as liquids above their melting temperature without the addition of any solvent. The Office cites paragraph [0623] of Rogier et al. and states that this reference “does not require the presence of water.”<sup>6</sup> In this paragraph Rogier et al. state that their composition comprises “a therapeutically-effective amount of a compound of Formula I-IV in association with at least one pharmaceutically-acceptable carrier, adjuvant or diluent.”<sup>7</sup> After synthesis, the compounds of Rogier et al. are in solid or crystalline forms,<sup>8</sup> which are combined with at least one carrier, adjuvant, or diluent to form the composition. From paragraph [0623], the Office concludes that the composition or compounds of Rogier et al. do not contain water. Rogier et al., however, disclose at paragraph [0717] that the adjuvants mixed with the compound are appropriate for the indicated route of administration. The compound may be admixed with lactose, sucrose, etc. and then tableted or encapsulated. Alternatively, formulations for parenteral administration may be in the form of aqueous or non-aqueous isotonic solutions or suspensions. Nowhere do Rogier et al. disclose or suggest a compound or composition that is an ionic liquid, i.e., a salt that forms a stable liquid above its melting temperature. In fact, the compounds of Formulas I-IV have melting temperatures that range from about 100°C to about 208°C.<sup>9</sup> Thus, the compounds and compositions of Rogier et al. are not liquid at room temperature (25°) in the absence of added liquid carriers, adjuvants, or diluents.

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<sup>6</sup> *Id.*

<sup>7</sup> Rogier, at paragraph [0623].

<sup>8</sup> *Id.*, at paragraph [0662] “yielding a white crystalline solid” and paragraph [0666] “yielding the desired produce as fine white clear needles.”

<sup>9</sup> *Id.*, see Examples 1-11 at paragraphs [0660]-[0696].

In summary, the Applicant respectfully submits that Rogier et al fail to disclose or suggest using an ionic liquid such as N,N-dimethylethanolammonium formate as the solvent or reaction medium in an enzyme-catalyzed reaction, as required in claims 57 and 58. Thus, not all of the required claim elements are disclosed or suggested by the prior art. Moreover, neither the disclosure of Rogier et al. nor knowledge generally available to those skilled in the art provides any reason or suggestion to modify the disclosure of Rogier et al. and arrive at the method of claims 57 and 58 with a reasonable expectation of success. Furthermore, it is respectfully submitted that even if a skilled person were somehow motivated to modify the disclosure of Rogier et al., that person would not arrive at the claimed invention without extensive undue experimentation. Accordingly, the Applicant respectfully submits that the method recited in claims 57 and 58 is not rendered obvious by Rogier et al. Claims 62-67 and claims 68-70, which depend from and incorporate the limitations of claims 57 and 58, respectively, likewise are not obvious in view of Rogier et al. for the same reasons stated above with respect to claims 57 and 58.

Because the reference relied on by the Office does not disclose or suggest the presently claimed method, the Office appears to be applying "hindsight reconstruction" by using the teaching of the Applicants' patent application as a guide for searching and analyzing the reference in the right way to arrive at the claims at issue. In this context, the Office has selectively picked compounds and phrases from Rogier et al. and combined them in the right way to arrive at the claimed invention. Such hindsight reconstruction is clearly contrary to the law.<sup>10</sup> The Office has simply not set-forth any sufficient art-based rationale as to why a person of skill in the art would have been motivated to modify the disclosure of Rogier et al. as suggested by the Office to arrive at the method recited in claims 57 or 58. The mere identification in the prior art individual elements or features of the method does not show that the combination as a whole is obvious.<sup>11</sup> Rather, to establish a *prima facie* case of obviousness based on a combination of elements in the prior art, the law requires a motivation to select the critical elements and combine them in the particular claimed manner to reach the

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<sup>10</sup> See *Orthopedic Equipment Co. v. United States*, 217 U.S.P.Q 193 (Fed. Cir. 1983).

<sup>11</sup> See *In re Dow Chemical*, 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988).

claimed invention.<sup>12</sup> Without this demonstration of the requisite motivation to make the Office's proposed modification, a *prima facie* case of obviousness has not been established.

In view of the above, Applicant respectfully requests withdrawal of the § 103 rejections of claims 57, 59, 62-60 in view of Rogier et al.

#### **IV. Conclusions**

In light of the foregoing, the Applicant requests entry of the claim amendments, withdrawal of the claim rejections, and solicits an allowance of all pending claims. The Examiner is invited to contact the undersigned practitioner should any issues remain unresolved.

Respectfully submitted,  
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<sup>12</sup> *In re Kahn*, 441 F.3d 977, 986 (Fed. Cir. 2006) (citing *In re Rouffet*, 149 F.3d 1350, 1355 (Fed. Cir. 1998)).